Calcium Homeostasis

Dr Doaa Abou-Bakr
Ass. Prof. of Physiology

- **By the end of this lecture the student will be able to:**

- Mention the normal total and ionized calcium levels.
- List its physiological significances.
- List the hormones involved in its regulation.
- List the functions of calcitonin, describe its regulation.
- Compare between the effects and mechanism of actions of each one.
- Summarize the mechanism of calcium homeostasis.

:Calcium in the body

Approximately 1 kg (1100 gm) (1.5% total body weight):

99 % in the skeleton (bone) (Ca^{++} bank)

0.9 % in the cells (soft tissue)

0.1 % in the extra cellular fluid (plasma)

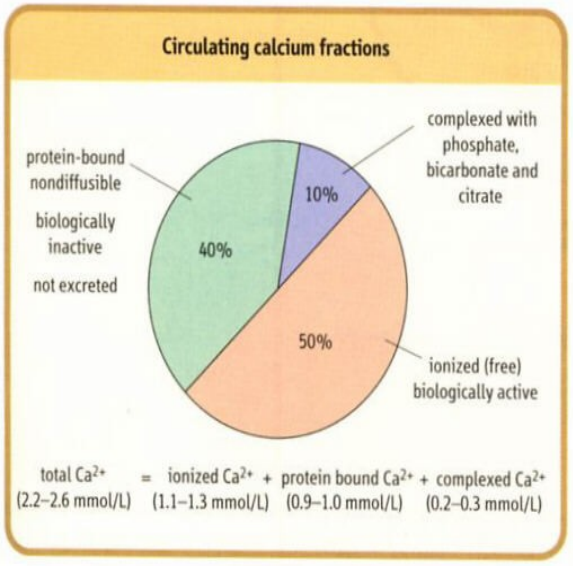
Bones serve as large calcium reservoirs, releasing calcium when its ECF concentration decreases.

:Plasma Ca^{++} level

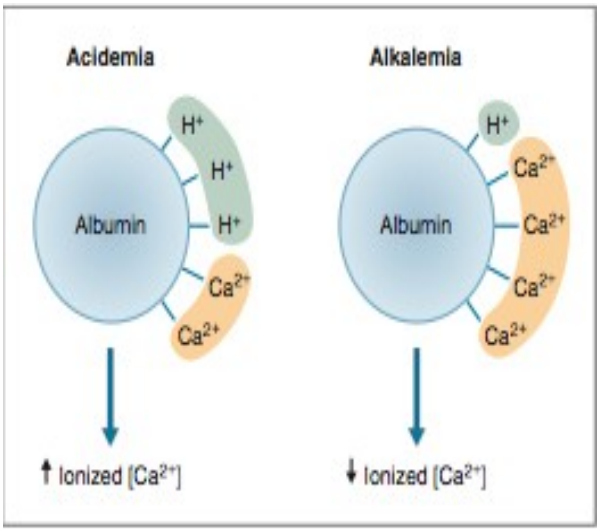
9-11
.mg/dl

Calcium transport in the blood

- **50%** as free ionized form.



- **40%** bound to protein (mainly albumin, some globulins).
- **10%** bound to anions in soluble complexes.



Ionized fraction depends on pH:

- Ca^{++} protein binding decreases as pH decreases

Ca^{++} protein binding increases as pH increases -

:Functions of Ionic Calcium

- **Calcium is necessary for:**

1- Bone and teeth formation hydroxyapatite crystals.

2- Neuromuscular excitability Ca++ stabilize voltage gated Na+ channeles

3- Synaptic transmission caused by Ca++ influx into presynaptic terminal.

4- Muscle contraction caused by Ca++ efflux from sarcoplasmic reticulum.

5- Hormone secretion as in insulin, catecholamines, ADH and oxytocin release.

6- Secondary messenger in many hormonal actions.

7- Blood coagulation Ca++ is a cofactor required at most factor activation steps.

8- Activation of some enzymes.

9- Cell proliferation, motility and ciliary action.

10- Maintain normal permeability of cell membrane and capillaries.

Calcium homeostasis = Maintenance of $^{++}$plasma free Ca

This done by action of **3 hormones** (Parathyroid H., Calcitonin and Calcitriol) on 3 target organs (Bone, .Intestine and Kidney)

- **Parathyroid hormone (PTH)**: Ca elevating hormone
- **Calcitriol (1,25 DHCC):** Ca elevating hormone
- **Calcitonin:** Ca lowering hormone

Calcitonin= Thyrocalcitonin

- Secreted by thyroid parafollicular cells.
- Polypeptide hormone (32 aa).
- Its action mediated by cAMP.
- Lowers Ca^{++} and PO_4^{---} levels by acting on bone and kidney.
- Antagonize PTH as regard Ca^{++} but similar to PTH as regard PO_4^{---}
- An increase in serum Ca^{++} level stimulates its secretion.
- Many GIT hormones e.g. Gastrin, Glucagon, CCK, Secretin. As well as Estrogen and Dopamine stimulate its release.

:**Actions:** Lowering Ca^{++} level

:On bone -1

Facilitate Ca deposition in bones (inhibits osteoclastic activity, decreasing its number & stimulates osteoblasts and increase its alkaline phosphatase activity).

:On kidney -2

- **inhibits α1 hydroxylase activity,** so Inhibits the activation of Vitamin D → decreased intestinal absorption of Ca^{++}

- **stimulates urinary excretion** of both Ca^{++} and PO_4^{-3}

Calcitriol = 1, 25 $(OH)_2$ D_3

:Obtained from

Diet*

:Synthesized in the body*

- Calcitriol is derived from a metabolite of cholesterol, 7-dehydro-cholesterol formed in the **liver**.

- Non-ezymatic breakage of the B-ring by ultraviolet light exposure in the **skin** form cholecalciferol (vitamin D3) which may also be obtained in the diet, *e.g.,* in vitamin D fortified milk.

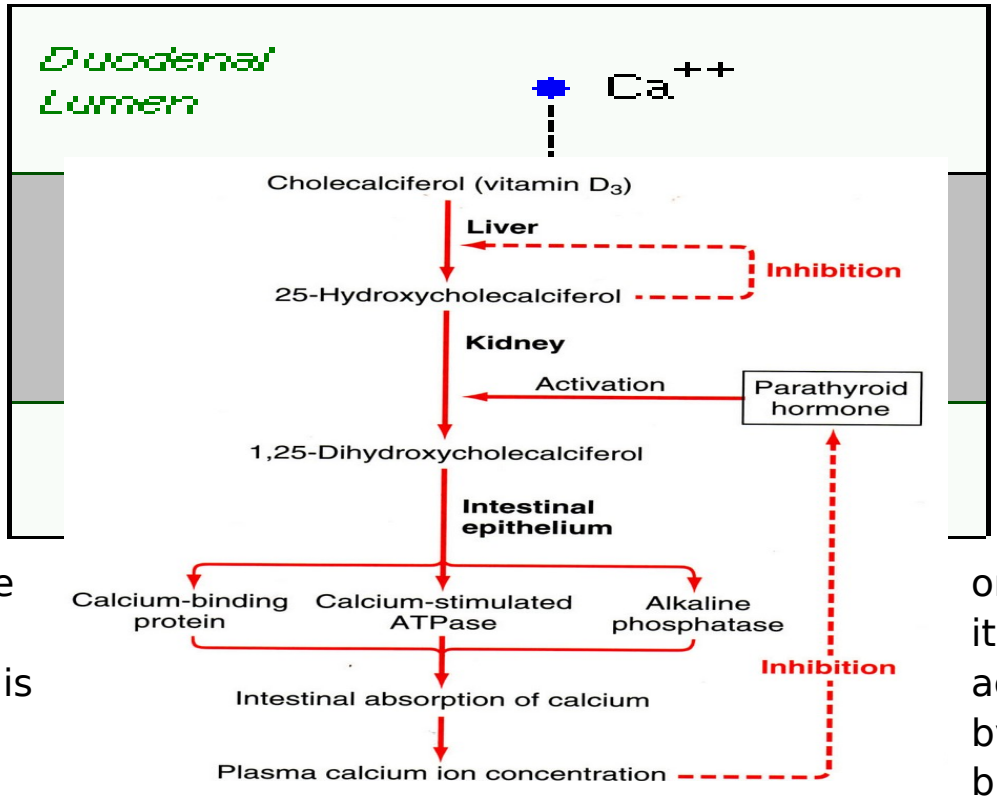
- **Liver** hydroxylates cholecalciferol on the side chain to form 25-hydroxycholecalciferol which is carried by the vitamin D carrier protein in serum to the kidney.

- In the **kidney** the molecule can be hydroxylated once or twice more to form the active hormone calcitriol or the inactive metabolites 24, 25-dihydroxycholecalciferol or 1α, 24, 25-trihydroxycholecalciferol.

PTH promotes 1α hydroxylation (activation), Calcitonin *
.promotes 24 hydroxylation (inactivation)

Plasma calcium concentration inversely regulates 1, 25 *
.DHCC

Actions: Being steroid hormone its action is by binding to an intracellular receptor. Elevating Ca level :



On Intestine (Main action): Increase absorption of Ca^{+} **-1** .$^{+}$ and PO_4^{-3} by increasing Calbindin D & Ca ATPase pump

On kidney: stimulates reabsorption of both Ca^{++} and **-2** PO_4^{-3}

On bone: Depends on Ca^{++} and PO_4^{-3} concentration **-3**

a- At high concentration: it stimulates osteoblastic .activity and bone mineralization

b- At low concentration: it stimulates osteoclastic .activity

:**IN SUMMARY:** Hormones affecting calcium homeostasis*

Parathyroid Hormone (PTH): Increases calcium ion levels by:

1. Stimulating osteoclasts.
2. Increasing intestinal absorption of calcium (indirectly).
3. Decreasing urinary calcium excretion.

Calcitonin (Thyrocalcitonin): Decreases calcium ion levels by:

1. Inhibiting osteoclasts.
2. Decreasing intestinal absorption of calcium (indirectly).
3. Increasing urinary calcium excretion.

Calcitriol (1, 25 DHCC): Increases calcium ion level by:

1- Increasing intestinal absorption of calcium.

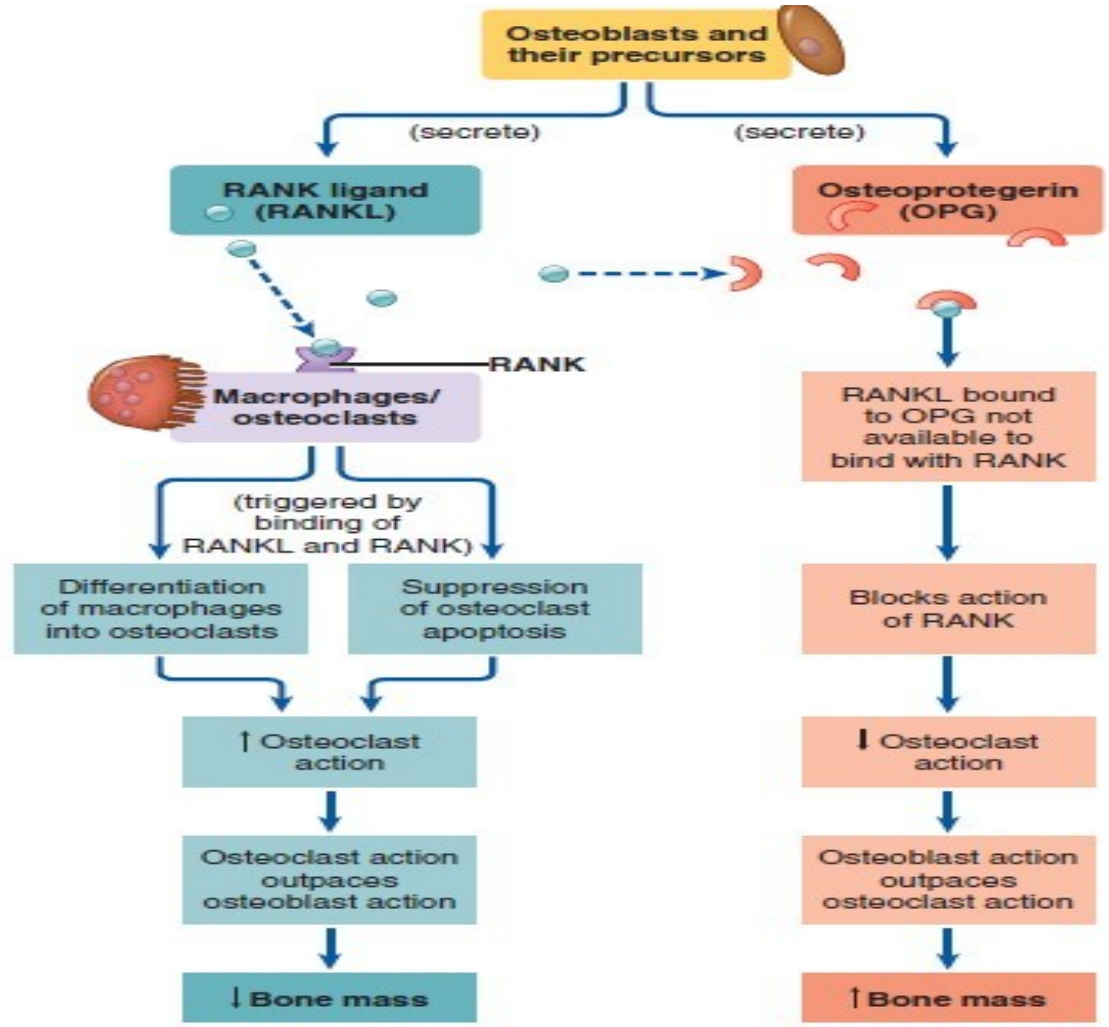
2- Decreasing urinary calcium excretion.

3- On bone: according to calcium level??????

Other hormones affecting bone and Ca^{++} :metabolism

Estrogens: slow down bone loss (stimulate osteoblast) (↑ OPG= osteoprotegerin gene).

Insulin: (increases bone formation).



Growth Hormone (increases Ca^{++}absorption).

Insulin like Growth factors (IGFs): (during fetal growth) as GH (increases Ca^{++} absorption).

Glucocorticoids: decreases Ca^{++} level by inhibiting its gut absorption & increasing renal excretion – decreases bone formation & inhibit osteoblast and stimulate osteoclast. Prolonged use of glucocorticoids produces osteoporosis (bone loss).

Role of osteoblasts in governing osteoclast development and activity

:Note

:Dietary sources of Calcium

-The most significant source: dairy products
-Sesame, Grape leaves, Molokhia, Green leafy vegetables such as broccoli
-Other sources of calcium are salmon ,sardines and Shellfish

Calcium absorption:

- It takes place in the duodenum
- Requires a protein carrier (Calbindin)

➢ **Factors increasing calcium absorption:**

1) Vitamin D (calcitriol): Stimulates synthesis of the carrier protein in the intestinal epithelial cells (at genetic level) →↑absorption
2) Acidity: increase Ca absorption
3) Lactose: present in milk increase Ca absorption
4) Form of calcium in food: Organic calcium salts are soluble →↑absorption

➢ **Factors decreasing calcium absorption:**

1) ↑pH (alkalosis): antacids decrease calcium absorption

↓calcium solubilization→ ↓absorption

2) Phytic acid, phosphate & oxalate in diet
3) Impairment of fat absorption causes presence of large amount of free fatty acids which react with calcium → ↓absorption
3) Form of calcium: inorganic calcium salts are insoluble →↓absorption